April 20, 2016

Onconova Announces Novel Dual Targeting of ARK5 and CDK4/6 by Pre-clinical Compound, ON 123300, in Presentation at 2016 American Association of Cancer Research (AACR) Annual Meeting

NEWTOWN, Pa., April 20, 2016 (GLOBE NEWSWIRE) -- Onconova Therapeutics, Inc. (Nasdaq:ONTX), a clinical-stage biopharmaceutical company focused on discovering and developing novel products to treat cancer, today announced the presentation of pre-clinical data for its first-in-class dual inhibitor of ARK5 and CDK4/6 at the 2016 AACR Annual Meeting being held April 16-20, 2016 at the Ernest N. Morial Convention Center in New Orleans, LA.

The poster presentation by investigators from the Icahn School of Medicine at Mount Sinai and the University of Nebraska Medical Center, compared the activity of ON 123300 to Ibrance® (palbociclib), an FDA approved CDK4/6 inhibitor. The studies revealed that both compounds could inhibit CDK4/6 but only ON 123300 targeted ARK5, a kinase that regulates cancer cell metabolism by increasing glutamine uptake. Using colorectal cancer cells as a model, the researchers demonstrated that ARK5 inhibition by ON 123300 reduced glutamine uptake leading to diminished cellular ATP levels. Most notably, the inhibitory activity of ON 123300 on ARK5 and CDK4/6 resulted in the activation of programmed cell death, while selective CDK4/6 targeting by palbociclib merely resulted in cytostasis.

"This pre-clinical poster adds to previous data demonstrating the important differentiating features of ON 123300," said Manoj Maniar, Ph.D., Senior Vice President for Product Development at Onconova. "We believe that the inhibition of ARK5 and induction of apoptosis by ON 123300 represent an improvement over the current generation of CDK4/6 inhibitors."

A full copy of the AACR poster titled, "Dual targeting of ARK5 and CDK4 pathways with ON 123300 as a therapeutic strategy," can be accessed by visiting "Posters" in the Investors and Media section of Onconova's website at www.onconova.com.

About Onconova Therapeutics, Inc.

Onconova Therapeutics is a Phase 3 clinical-stage biopharmaceutical company focused on discovering and developing novel products to treat cancer. Onconova's clinical and pre-clinical stage drug development candidates are derived from its extensive chemical library and are designed to work against specific cellular pathways that are important in cancer cells, while causing minimal damage to normal cells. In addition to rigosertib, the Company's most advanced product candidate, two other candidates are at clinical stage, and several candidates are in pre-clinical stages. For more information, please visit http://www.onconova.com.

About CDK4/6

Cyclin-dependent kinases 4 and 6, or CDK4/6, are enzymes that regulate cell cycle progression. These proteins are activated in response to mitogenic signaling and respond by driving cells into the DNA synthesis phase of the cell cycle. Several CDK4/6 specific inhibitors are in clinical development and one such molecule, Ibrance® (palbociclib), has received FDA approval in combination with the aromatase inhibitor, letrozole. As single agents, the current CDK4/6 inhibitors are cytostatic and may require the addition of drugs targeting other signaling pathways in order to convert cytostatic effects into cancer cell death.[1]

About ARK5

ARK5, or AMPK-related kinase 5, is an enzyme encoded by the *NUAK1* gene. ARK5 is activated by AKT and is thought to support macromolecule biogenesis while also promoting tumor invasion and metastasis.[2] Recent evidence suggests an important cooperative function for ARK5 in c-MYC dysregulated cellular metabolism.[3] Overexpression of ARK5 has been observed in numerous cancers, including multiple myeloma.[4]

References

[1]Sherr CJ et al. Targeting CDK4 and CDK6: From Discovery to Therapy. *Cancer Discov*. 2016 Apr;6(4):353-67.

[2]Suzki A et al. ARK5 is a tumor invasion-associated factor downstream of Akt signaling. *Mol Cell Biol.* 2004 Apr;24(8):3526-35.

[3]Liu L et al. Deregulated MYC expression induces dependence upon AMPK-related kinase 5. *Nature*. 2012 Mar 28;483 (7391):608-12.

[4]Perumal D et al. Dual Targeting of CDK4 and ARK5 Using a Novel Kinase Inhibitor ON123300 Exerts Potent Anticancer Activity against Multiple Myeloma. *Cancer Res*. 2016 Mar 1;76(5):1225-36.

Forward Looking Statements

Some of the statements in this release are forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, Section 21E of the Securities Exchange Act of 1934, as amended, and the Private Securities Litigation Reform Act of 1995, which involve risks and uncertainties. These statements relate to future events or Onconova Therapeutics, Inc.'s future operations, clinical development of Onconova's product candidates and presentation of data with respect thereto, regulatory approvals, expectations regarding the sufficiency of Onconova's cash and other resources to fund operating expenses and capital expenditures, Onconova's anticipated milestones and future expectations and plans and prospects. Although Onconova believes that the expectations reflected in such forward-looking statements are reasonable as of the date made, expectations may prove to have been materially different from the results expressed or implied by such forward-looking statements. Onconova has attempted to identify forward-looking statements by terminology including "believes," "estimates," "anticipates," "expects," "plans," "intends," "may," "could," "might," "will," "should," "approximately" or other words that convey uncertainty of future events or outcomes. These statements are only predictions and involve known and unknown risks, uncertainties, and other factors, including Onconova's need for additional financing and current plans and future needs to scale back operations if adequate financing is not obtained, the success and timing of Onconova's clinical trials and regulatory approval of protocols, and those discussed under the heading "Risk Factors" in Onconova's most recent Annual Report on Form 10-K and quarterly reports on Form 10-Q.

Any forward-looking statements contained in this release speak only as of its date. Onconova undertakes no obligation to update any forward-looking statements contained in this release to reflect events or circumstances occurring after its date or to reflect the occurrence of unanticipated events.

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